

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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| Applicant's or agent's file reference<br><b>KOPCHIC8APCT</b> | <b>FOR FURTHER ACTION</b><br>see Form PCT/ISA/220<br>as well as, where applicable, item 5 below. |  |
| International application No.<br><b>PCT/US2004/021944</b>    | International filing date (day/month/year)<br><b>08/07/2004</b>                                  | (Earliest) Priority Date (day/month/year)<br><b>08/07/2003</b> |
| Applicant<br><br><b>OHIO UNIVERSITY</b>                      |  |  |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 10 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

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International application No.  
PCT/US2004/021944

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ in written format
- ☒ in computer readable form
- c. time of filing/furnishing
- ☐ contained in the international application as filed
- ☐ filed together with the international application in computer readable form
- ☒ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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International application No.  
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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 4-16 (all completely), 17-31 (all partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-30 (all partially), 31 (completely)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-30 (all partially), 31 (completely)

Invention 1: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-11

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2. claims: 1-30 (all partially), 32 (completely)

Invention 2: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-29

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3. claims: 1-30 (all partially), 33 (completely)

Invention 3: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-97

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4. claims: 1-30 (all partially), 34 (completely)

Invention 4: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-130

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5. claims: 1-30 (all partially), 35 (completely)

Invention 5: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-105

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6. claims: 1-30 (all partially), 36 (completely)

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 6: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-38  
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7. claims: 1-30 (all partially), 37 (completely)

Invention 7: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-41  
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8. claims: 1-30 (all partially), 38 (completely)

Invention 8: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-43  
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9. claims: 1-30 (all partially), 39 (completely)

Invention 9: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-61  
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10. claims: 1-30 (all partially), 40 (completely)

Invention 10: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-9  
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11. claims: 1-30 (all partially), 41 (completely)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 11: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-138

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/021944A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, BIOSIS, Sequence Search, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| X          | MERCHED A ET AL: "APOLIPOPROTEIN AIV<br>CODON 360 MUTATION INCREASES WITH HUMAN<br>AGING AND IS NOT ASSOCIATED WITH<br>ALZHEIMER'S DISEASE"<br>NEUROSCIENCE LETTERS, LIMERICK, IE,<br>vol. 242, no. 2,<br>13 February 1998 (1998-02-13), pages<br>117-119, XP000863724<br>ISSN: 0304-3940<br>the whole document<br>-----<br>-/-- | 1-3,<br>17-31         |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

10 January 2005

Date of mailing of the international search report

28-06-2005

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| X          | <p>MICHIKAWA Y ET AL: "Aging-dependent large accumulation of point mutations in the human mtDNA control region for replication"</p> <p>SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, 22 October 1999 (1999-10-22), pages 774-779, XP002179334</p> <p>ISSN: 0036-8075</p> <p>the whole document</p> <p>-----</p>       | 1-3,<br>17-31         |
| X          | <p>LIO D ET AL: "Gender-specific association between -1082 IL-10 promoter polymorphism and longevity"</p> <p>GENES AND IMMUNITY, vol. 3, no. 1, February 2002 (2002-02), pages 30-33, XP008039832</p> <p>ISSN: 1466-4879</p> <p>the whole document</p> <p>-----</p>  | 1-3,<br>17-31         |
| X          | <p>MOCCHIGIANI EUGENIO ET AL: "MTmRNA gene expression, via IL-6 and glucocorticoids, as potential genetic marker of immunosenescence: Lessons from very old mice and humans"</p> <p>EXPERIMENTAL GERONTOLOGY, vol. 37, no. 2-3, January 2002 (2002-01), pages 349-357, XP002312292</p> <p>ISSN: 0531-5565</p> <p>the whole document</p> <p>-----</p> | 1-3,<br>17-31         |
| X          | <p>WO 03/000861 A (LEHRER-GRAIWER JOSH ; APFELD JAVIER (US); DILLIN ANDREW (US); GARIGAN) 3 January 2003 (2003-01-03)</p> <p>Methods to identify lifespan associated genes; gene therapy involving said genes</p> <p>the whole document</p> <p>-----</p>   | 1-3,<br>17-31         |
| X          | <p>US 6 025 194 A (FUNK WALTER)</p> <p>15 February 2000 (2000-02-15)</p> <p>GC6 gene as cell senescence marker gene</p> <p>the whole document</p> <p>-----</p>   | 1-3,<br>17-31         |
|            | -/--   |                       |



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/021944

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | <p>ZHOU YIHUA ET AL: "A mammalian model for Laron syndrome produced by targeted disruption of the mouse growth hormone receptor/binding protein gene (the Laron mouse)"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 94, no. 24, 25 November 1997 (1997-11-25), pages 13215-13220, XP002312293</p> <p>ISSN: 0027-8424</p> <p>The Laron or GHR/BP-deficient mouse is proposed as a useful animal model in the study of senescence</p> <p>page 13220</p> <p>-----</p> | 1-3,<br>17-31         |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/021944

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|---|---------------------|----------------------------|---------------------|
| WO 03000861                               | A | 03-01-2003          | CA 2451247 A1              | 03-01-2003          |
|   |   |                     | EP 1406489 A2              | 14-04-2004          |
|   |   |                     | WO 03000861 A2             | 03-01-2003          |
|   |   |                     | US 2003190312 A1           | 09-10-2003          |
| -----                                     |   |                     |                            |                     |
| US 6025194                                | A | 15-02-2000          | AU 1701599 A               | 07-06-1999          |
|   |   |                     | WO 9925878 A2              | 27-05-1999          |
| -----                                     |   |                     |                            |                     |

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